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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,627	04/17/2001	Robert A. Scott	6514-11-BHJ	7296

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EXAMINER
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SHEIKH, HUMERA N

ART UNIT	PAPER NUMBER
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1615

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.



Art Unit: 1615

## **DETAILED ACTION**

### **Status of the Application**

Receipt of the Request for Continued Examination (RCE) under 37 CFR 1.114, the Amendment, Applicant's Arguments/Remarks and Information Disclosure Statement (IDS), all filed 06/04/04 and the request for extension of time (3 months-granted) and Notice of Appeal, both filed 01/08/04 is acknowledged.

Claims 1-21, 24, 25 and 29-33 are pending. Claims 22-23 and 26-28 have been cancelled. Claims 1-21, 24, 25 and 29-33 are rejected.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**Claims 1-5, 7-10, 13-21, 24, 25 and 29-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hatano *et al.* (EP 0754 452 A2).**

The instant invention is drawn to a drug delivery composition consisting essentially of a HPMC capsule provided with a single aqueous coating for delivering drug in the small intestine or colon.

Hatano *et al.* teach a coated capsule containing an acidic substance, a polymer film and an enteric coating, for medicament delivery to any site between the upper part of the small intestine and the lower part of the large intestine in the digestive tract (see pg. 3, lines 7-10). Hatano *et al.* teach that the enteric coating film protects the pharmaceutical preparation in the stomach and dissolves in the upper part of the small intestine, allowing the digestive juices to gradually penetrate and dissolve the acidic substance in the hard capsule (pg. 3, lines 11-19). According to Hatano *et al.*, the pharmaceutical agents in the capsule can be selectively released at any desired site between the jejunum and the rectum and any type of capsule can be used in the invention, including HPMC capsules (pg. 4, lines 6-20). Hatano *et al.* teach that the enteric polymer used for the enteric coating film must be soluble in a pH higher than 5 and includes a cellulose derivative, an acrylic polymer, a maleic copolymer, a polyvinyl derivative, shellac and the like among the polymers used for the enteric coating (pg. 4, lines 46-49). Among the exemplary polymers, Hatano *et al.* includes HPMC, methyl acrylate-acrylic acid copolymer, methyl acrylate-methacrylic acid copolymer and PVAP (pg. 4, lines 50-58 and pg. 5, lines 1-9).

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The Examiner, for the purpose of the invention, considers cellulose ester, which is mentioned in claims 15 of the present application as a component of the coating, as a cellulose derivative.

Hatano *et al.* teach that the amount of the enteric coating film is from 10-400% by weight based on the weight of the hard capsule (pg. 5, lines 41-46), and that the medicament in the capsule is not limited as long as it is orally administrable (pg. 8, lines 3-9). Hatano *et al.* teach that preferable solvents for the coating solution are water and alcohol (pg. 9, lines 8-19). Additionally, Hatano *et al.* teach that a sealing means can be provided around a joint of a body and a cap of the hard capsule and explains that the sealing agent can be any substance able to make the capsule's surface smooth at the joint, such as a water-soluble or insoluble polymer, a low pH-soluble or enteric polymer, a saccharide or the like (pg. 9, lines 23-55).

Thus, Hatano *et al.* provide a HPMC capsule provided with an enteric coating for delivering a drug in the small intestine or colon. Although Hatano *et al.* contemplates a capsule coated with multiple coatings, the reference teaches that only one enteric coating, which is soluble in an aqueous medium at pH higher than 5, is applied to the capsule.

**Claims 6, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hatano *et al.* (EP 0754 452 A2) as applied to claims 1-5, 7-10, 13-21, 24, 25 and 29-33 above and further in view of Watts (WO 95/35100).**

The teachings of Hatano *et al.* are delineated above. Hatano *et al.* do not teach the inclusion of a redox-sensitive material in the coating of the HPMC capsule and do not teach cellulose acetate trimellitate (CAT).

Watts discloses a drug delivery composition for delivering a drug to the colonic region, comprising a coated starch capsule containing the drug (see pg. 3, lines 25-29). Watt teaches that the coating may be pH-sensitive, redox-sensitive or sensitive to the particular enzymes or bacteria, so that the capsules do not release the drug until it is in the colon (pg. 5, lines 9-14). Watts teaches that preferred coating materials are those which dissolve at a pH of 5 or above, including CAT, HPMC, PVAP, shellac and cellulose esters, and that especially preferred materials are methylmethacrylates or copolymers of methacrylic acid and methylmethacrylate (pg. 5, lines 20-30 and pg. 6, lines 1-22). Watts explains that, because of the high presence of microbial anaerobic organisms providing reducing conditions in the colonic region, the coating may comprise a redox-sensitive material, such as azopolymers, which are broken down enzymatically, or disulphide polymers (pg. 6, lines 24-30 and p. 7, lines 1-2). It is the position of the Examiner that one of ordinary skill in the art would determine the optimal amount of the coating according to the size of the capsule by routine experimentation.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the drug delivery system disclosed by Hatano *et al.* by including a redox-sensitive material in the coating of the HPMC capsule, as taught by Watts, and applying the suitable coating in the optimal range determined by routine experimentation, before or after filling the capsule with the caplet, to ensure a complete disintegration of the coating in the small intestine or the colon and prevent drug leaking in the stomach. The expected result would be an improved drug delivery composition. Based on the teachings of Hatano *et al.*, that any kind of medicament can be delivered to any desired site between the upper part of the small intestine and the lower part of the large intestine in the digestive tract, by controlling the amount

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and the kind of polymers used for the coating of the HPMC capsule, one of ordinary skill in the art would have a reasonable expectation that the HPMC capsule device of the present application would successfully deliver drugs to the small intestine or colon. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art.

### ***Response to Arguments***

Applicant's arguments filed 06/04/04 have been fully considered but they are not persuasive.

Firstly, Applicant argued, "Independent Claim 1 is limited to exclude additional coatings that do not materially alter the basic characteristic of a single aqueous coating and is therefore allowable over the cited references."

This argument has been fully considered, but was not found to be persuasive. Hatano *et al.* teach that only one enteric coating is applied to the capsule. Hatano *et al.* teach at page 8, lines 38-40, that the intermediate layer *can be* provided, *if desired*, suggesting that the intermediate layer is an optional component and therefore suggests a single enteric coating layer.

Secondly, Applicant argued, "Hatano *et al.* does not contemplate a single aqueous coating as recited in independent Claim 1. Hatano *et al.* teach that each capsule is coated with two separate layers (enteric coating and a polymer film soluble at low pH)."

This argument has been fully considered, but was not found to be persuasive. The prior art teaches an HPMC capsule for release into the intestines, as similarly desired by Applicant. Burden is shifted to Applicant to demonstrate that any additional layer contemplated by the prior

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art would be detrimental to the formulation, since the prior art clearly teaches a similarly formulated HPMC capsule for release of medicament at any desired site in the intestines.

### Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays from 8:00 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

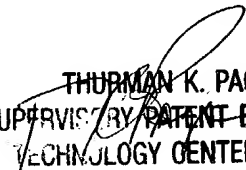
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

*H. N. Sheikh HNS.*

Patent Examiner

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August 30, 2004

  
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